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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/790,488	SHERMAN ET AL.	
	Examiner	Art Unit	
	Timothy E. Betton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38 and 45-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38 and 45-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed 9 November 2007 have been acknowledged and duly recorded.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant invention.

Applicants' assert that the specification describes the combination of CCI-779 with an aromatase inhibitor for [the] treatment of breast cancer. Applicants' attention is directed to Example 1 of the instant specification (pgs 13 and 14). Within this embodiment, applicant discloses data which presents no clear indication of what parameters constitute a complete response, a partial response, or data indicative of a stable disease state. Granted, due to the nature of the invention, toxicity monitoring is of high concern. However, the scope of the claimed invention is not drawn to a study/trial based solely on a determination of toxicity. The instant claim 1 cites specifically, ' a method of treating a neoplasm'. The skilled artisan knows in the well-known art of treating any neoplasm, there is a multiplicity of factors to be considered in sufficiently determining an effective treatment. Neoplasms present with variable etiologies, properties, characteristics and susceptibilities as would be fully apparent to the skilled artisan. Applicants' claim a single compound/composition combination formulation which can singlehandedly eradicate a neoplasm. However, the specification is silent in regard to Examples clearly pointing to this limitation as the central issue or a significant factor in adequately claiming the inventive objective.

Applicants' further assert that the cited application requires a combination of an antineoplastic alkylating agent with the mTOR inhibitor. It is only in addition to that combination that a further component may be added. In the claimed invention of this application, no antineoplastic alkylating agent is required. However, the Dukart et al. reference clearly discloses and teaches variable pharmaceutical combinations and combination/formulation therapy (abstract only, paragraph 12 and 58). It would not be so apparent to the skilled artisan that *'only in addition' to* that combination (i.e., combination of an antineoplastic alkylating agent with the mTOR inhibitor). Further, the instant specification does not adequately elucidate this claimed limitation nor do the instant claims disclose this limitation in view of the inventive objective of present invention.

For the reasons already of record, the 112, 1st paragraph rejection is maintained, the 102(e) rejection is maintained, and the 103(a) rejection is maintained, respectively.

Claim Rejection- 35 USC §112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-34, and 36-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of breast cancer using the claimed combinations, does not reasonably provide enablement for treatment of all neoplasms of any type. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Exparte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims

The Board also stated that the level of skill in the pertinent art is high; the results of experimentation in treating a neoplasm in a mammal in need thereof are unpredictable. While all these factors are considered, a sufficient amount for a prima facie case is discussed below:

The nature of the invention

This invention relates to treatment of neoplasms.

The amount of direction or guidance provided

The amount of direction or guidance provided is insufficient in regard to a proper explanation as to how treatment directed toward neoplasms of any type. The instant specification discloses general extrapolations of the subject matter of claimed invention. Quantitative direction and/or guidance is lacking in view of the scope and variable susceptibilities of claimed invention.

The quantity of experimentation necessary and state of the art

The quantity of experimentation necessary is high. Further studies, research and development are required due to insufficient evidence in the instant specification to support a proper scope of enablement of current invention. The instant specification discloses no such examples of experimentation. The experimentation yields no quantifiable evidence (comparative data of disclosure of studies on various etiologies of neoplasms or neoplasm types via due experimentation).

The presence or absence of working example

A practicing working example disclosing an embodiment of the central issue of invention directed toward a method of treating any neoplasm type is absent.

One of ordinary skill in the pertinent art would not be readily inclined to reasonably envision the scope of enablement in view of the two examples disclosed within the instant specification.

The predictability in the art

The level of unpredictability is high in the art. The instant specification does not support the due experimentation necessary for the embodiments of claimed invention to be predictable.

For example, the term neoplasm/solid tumor encompasses three distinctly different categories of tumors: (1) sarcomas, those that arise from connective or supporting tissues, such as bone or muscle; (2) carcinomas, those that arise from glandular tissues and epithelial cells; and (3) lymphomas, those that arise from the lymphoid organs, such as the lymph nodes, spleen or thymus. There are distinct etiologies and pathophysiological differences between these three categories of solid tumor would not have imbued the skilled artisan with a reasonable expectation of success in treating any one or more of these neoplasm types.

The pertinent art still deems neoplasmic conditions/solid tumors as unpredictable in their clinical behavior (Giuseppe et al., Pulmonary Epithelial-Myoepithelial Tumor of Unproven Malignant Potential: Report of a case and Review of the Literature, Mod Pathol (2001), 14(5): 521-526, printed pages 1-8, especially page 2, immediate paragraph under Full Table).

Claim Rejection- 35 USC §102(e)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1- 41 and 45-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Dukart et al. (USPGPUB 2003/0008923 A1).

Dukart et al. teach neoplasms generally or four specific neoplasmic conditions, i.e., colon, neuroblastoma, glioblastoma, rhabdomyosarcoma [0009], [0010], [0057].

Dukart et al. teach CCI-779 [0006, 0007].

Dukart et al. teach 42-O- (2-hydroxy) ethyl rapamycin ([0032, 0034], (referenced claims 30 and 34)).

Dukart et al. teach letrozole [0064].

Dukart et al. teach a practicing method of administering subtherapeutically effective amounts (page 7, patented claim 27).

Dukart et al. teach neoplasms generally or four specific neoplasmic conditions, i.e., colon, neuroblastoma, glioblastoma, rhabdomyosarcoma [0009], [0010], [0057]. Dukart et al. also teach renal cancer, soft tissue sarcoma, breast cancer, neuroendocrine tumor of the lung, cervical cancer, uterine cancer, head and neck cancer, glioma, non-small cell lung cancer, prostate cancer, pancreatic cancer, lymphoma, melanoma, small cell lung cancer, ovarian cancer, colon cancer, esophageal cancer, gastric cancer, leukemia, colorectal cancer, and unknown primary cancer (page 7, patented claims 1-22).

Dukart et al. teach variable pharmaceutical combinations and combination/formulation therapy (Abstract, [0012], [0058]).

Dukart et al. teach compositions and products which fully anticipate the subject matter of claimed invention. As shown above, Dukart et al. teach the exact therapeutic agents as disclosed in claimed invention.

Thus, Dukart et al fully anticipates the central issue of claimed invention.

The claim is anticipated by the reference. No question of obviousness is present. In other words, for anticipation under 35 USC 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present.

Claim Rejection- 35 USC §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dukart et al. (USPGPUB 2003/0008923) in view of Bertelsen et al. (WO/2001/074335).

Dukart et al. teaches subject matter as applied above.

Bertelsen et al. teach novel pharmaceutical kit comprising controlled release pharmaceutical compositions for oral use containing midodrine and/or its active metabolite desglymidodrine and a relatively fast onset composition. The controlled release compositions are designed to release midodrine and/or desglymidodrine after oral intake in a manner which enables absorption to take place in the gastrointestinal tract so that a relatively fast peak plasma concentration of the active metabolite desglymidodrine is obtained followed by a prolonged and relatively constant plasma concentration of desglymidodrine. Also disclosed is a method for treated orthostatic hypotention and/or urinary incontinence, the method comprising administration to a patient in need thereof of an effective amount of midodrine and/or desglymidodrine in a kit according to the invention.

Thus, it would be prima facie obvious to one of ordinary skill in the art of pharmaceuticals to at once recognize the reasonable expectation of success if the subject matter

of Bertelsen et al was incorporated with the subject matter of Dukart et al. Dukart et al. teach every element of claimed invention with the exception of a pharmaceutical system or kit. Thus, the invention of Bertelsen et al. would be the motivation to combine due to the facilitation of administration and compliance via the use of any pharmaceutical kit, which requires the patient to adhere to a regimen of poly-pharmacy.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information

for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

SHENGJUN WANG
PRIMARY EXAMINER

S. Wang